REMARKS

I. Support for the Amendments

Claims 1, 3, 4, 9, 11, and 14 have been amended. New claim 15 has been added. In order to further prosecution in a timely manner, claim 2 has been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

Support for amended claims 1, 3, 4, 9, 11, and 14 and for new claim 15 can be found in the original specification and claims. Additional support for amended claims 1 can be found, e.g., from page 13, line 5, to page 19, line 11; and in the Examples. Additional support for amended claim 9 can be found, e.g., from page 45, line 29, to page 47, line 27; and in the Examples (particularly in Example 3). Additional support for amended claim 14 can be found, e.g., from page 24, line 33, to page 25, line 21; and in the Examples. Additional support for new claim 15 can be found, e.g., from page 24, line 33, to page 25, line 4; from page 25, line 26, to page 29, line 30; and in the Examples. The amendments to claims 3, 4, and 11 are largely a matter of form.

II. Status of the Claims

Claims 1-14 were originally in the application, with claim 1 being the independent claim. Claims 1-14 were subject to an Election/Restriction Requirement, and claims 1-7, 9, 11, and 14 (Group I) were elected with traverse.

In the Office Action mailed December 17, 2003, the Examiner rejected claims 1-7, 9, 11, and 14, which were all the remaining claims.

Claims 1, 3-7, 9, 11, 14, and 15 are presently in the application. Claim 1 is the independent claim. Claims 3-7, 9, 11, 14 and 15 are now dependent on claim 1 or on a claim that is ultimately dependent on claim 1. New claim 15 has been added. In order to further prosecution in a timely manner, claim 2 has been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

III. Acknowledgement of Foreign Priority Claim

The Examiner has acknowledged the claim for foreign priority and the receipt of all certified copies of priority documents. Applicants thank the Examiner for acknowledging the foreign priority claim.

IV. Remarks Concerning the Information Disclosure Statement

The Examiner has signed and initialed the PTO Forms 1449 filed on February 27, 2002, and on February 28, 2003, but did not acknowledge the Information Disclosure Statements filed on April 1, 2002 (received at the USPTO on April 11, 2002), and on December 4, 2003 (received at the USPTO on December 11, 2003). Applicants wish to draw the Examiner's attention to these Information Disclosure Statements and respectfully request the Examiner's consideration of the references cited therein.

V. The Rejection of Claims 1-4, 11 and 14 under 35 U.S.C. §101 is Accommodated

The Examiner has rejected claims 1-4, 11, and 14 under 35 U.S.C. §101 (p.3; par. 7). The Examiner alleges:

> Claims 1-4, 11, and 14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter, a protein of SEQ ID NO: 1, a DNA encoding the protein. Since these molecules can be found in nature, the claims read on a product of nature. Products of nature do not constitute statutory subject matter. It is suggested that the word "isolated" or "purified" be used to amend the claims to overcome this rejection. (P. 3; par. 7.)

Applicants have added the phrase "isolated" to claims 1, 3, 4, 11, and 14 in accordance with the Examiner's suggestions.

In order to further prosecution in a timely manner, claim 2 has been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

Applicants respectfully submit that the amendments to claims 1, 3, 4, 11, and 14 accommodate the Examiner's rejection of these claims under 35 U.S.C. §101, thereby placing these claims in condition for allowance.

VI. The Rejection of Claims 1-7, 9, 11 and 14 under 35 U.S.C. §101 and 35 U.S.C. §112, First Paragraph, is Traversed and Partly Rendered Moot

The Examiner has rejected claims 1-7, 9, 11, and 14 under 35 U.S.C. §101 (pp.3-5; par. 9) and under 35 U.S.C. §112, first paragraph (pp. 5-7, par. 10). Applicants respectfully disagree.

With respect to 35 U.S.C. §101, the Examiner alleges:

> Claims 1-7, 9, 11, and 14 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1-7, 9, 11, and 14 are drawn to a protein comprising SEQ ID NO: 1 or its homologues, a DNA encoding the proteins, a method of producing the proteins, and a method of determining a ligand to the proteins. The claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. A specific and substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" context of use for the claimed invention which does not requires further research.

The specification asserts that **the present invention relates to a human brain-derived G protein coupled receptor (GPCR**; lines 7-9 of page 1). The specification discloses the expression of the protein of SEQ ID NO: 1 in various tissues (Example 2), which shows **high expression in the heart, kidney, and testis** (Fig. 4 and Table 1). **Nonetheless, the specification fails to disclose the biological functions or any physiological significance of the protein of SEQ ID NO: 1 or the DNA encoding the protein.** The specification fails to disclose a specific and substantial utility for the claimed invention.

The specification further asserts that the protein of the present invention and the DNA encoding the protein are **useful for the prevention and/or treatment of a list of numerous diseases** (the middle of page 55) and the cDNA of the present invention is useful as a gene diagnostic agent (bottom of page 58). These asserted utilities are not specific and substantial because they do not identify or reasonably confirm a "real world" context of use. **The specification neither identifies the biological functions of the claimed protein and DNA nor any diseases that are associated with the claimed molecules. Clearly, further research would be required to determine the functions of the claimed molecules or to identify a disease that can be treated or diagnosed with the claimed molecules.** See *Brenner v. Manson,* 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966), noting that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

The invention also lacks a well-established utility. A well-established utility is a specific, substantial, and creditable utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. While the specification asserts that the present invention is related to a human GPCR, there is no sufficient evidence indicating that the protein of the present invention is a truly functional GPCR. No art of record discloses or suggests any property or activity for the claimed molecules such that another non-asserted utility would be well-established for the compounds. (Pp. 4-5, par. 9; emphasis added.)

With respect to 35 U.S.C. §112, first paragraph, the Examiner alleges:

Claims 1-7, 9, 11, and 14 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the

reasons set forth above, one skilled in the art clearly would not know how to make/use the claimed invention.

Furthermore, even if the protein of SEQ ID NO: 1 or the DNA of SEQ ID NO: 2 that encodes SEQ ID NO: 1 were to have a patentable utility, the instant disclosure would not be found to be enabling for the full scope of the claimed invention.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman,* 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands,* 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 1 recites a protein which comprises the same or substantially the same amino acid sequence SEQ ID NO: 1, whereas claim 2 recites a partial peptide of the protein of claim 1. Claims 3 and 14 recite a DNA that encodes the protein of claim 1 or hybridises to the DNA encoding the protein *of* claim 1. However, other than the protein of SEQ ID NO: 1 and the DNA of SEQ ID NO: 2 that encodes the protein, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claim. The disclosure has not shown (i) which portions of SEQ ID NO: 1 or SEQ ID NO: 2 are critical to the activity of the protein of SEQ ID NO: 1; and (ii) what modifications (e.g., substitutions, deletions or additions) one can make to SEQ ID NO: 1 will result in protein mutants with the same functions as the protein *of* SEQ ID NO: 1. The state of the art (See, e.g., Ngo, et al, *The Protein Folding Problem and Tertiary Structure Prediction,* 1994, Merz, et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495) is such that the relationship between sequence of a protein and its activity is not well understood and is not predictable. Excising out portions of a protein or modifications to a protein, e.g., by substitutions or deletions, would often result in deleterious effects to the overall activity and effectiveness of the protein.

Accordingly, the disclosure fails to enable such a myriad of the claimed protein and DNA molecules that not only vary substantially in length but also in amino acid/nucleic acid composition and fail to provide any guidance to those skilled generally on how to make and use the genus of protein and DNA molecules. Thus, it would require undue experimentation for one skilled in the art to make and use the claimed genus of protein and DNA molecules embraced by the instant claims. (Pp. 5-7, par. 10; emphasis added.)

Applicants respectfully disagree with the Examiner and traverse the rejections under 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph.

Applicants believe that the present invention is well supported by the specific, substantial, and credible asserted utility. Applicants wish to draw to Examiner's attention to Example 3 in the specification (page 86, line 6, to page 87, line 2). Example 3 demonstrates the reactivity of the protein of the present invention (AQ27 of SEQ ID NO:1) with respect to Met-Enkephalin-Arg-Phe amide.

Moreover, the physiological function of the Met-Enkephalin-Arg-Phe amide was known to those of skill in the art. The Met-Enkephalin-Arg-Phe amide is considered to be a ligand for AQ27 because of its reactivity.

For example, the Examiner's attention is directed to the discussion of the physiological function of the ligand, Met-Enkephalin-Arg-Phe, in Wong et al. (Comp. Biochem. Physiol. 18C (1): 175-179 (1985)), a copy of which is enclosed with the Information Disclosure Statement filed herewith. More specifically, Wong discloses that YGGFMRFamide (Met-Enkephalin-Arg-Phe amide) produces cardiovascular effects in response to i.c.v. injection into a mammalian brain (see, e.g., p. 176, right-hand column, ll. 35-37). It would be reasonable for a skilled person to recognize that if a ligand has a certain biological function, a receptor to which the ligand binds is also associated with such biological function. Accordingly, at the time the present application was filed, the AQ27 protein was believed to be associated with circulatory diseases, such as those described on page 55, lines 31-33 of the present specification. Similarly, with respect to the physiological activity of YGGFMRFamide, Wong also describes that "YGGFMRFamide was more potent...in relaxing the rectum" (p. 175, right-hand column, ll. 11-13). Therefore, Applicants respectfully submit that the present invention is supported by a specific, substantial, and credible asserted utility.

In order to further prosecution in a timely manner, claim 2 has been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

Applicants respectfully submit that the amendments to claims 1, 3-7, 9, 11, and 14 fulfill the requirements of 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph, and assert these claims are in condition for allowance. Applicants respectfully request the Examiner's reconsideration of claims 1, 3-7, 9, 11, and 14 accordingly.

VII. The Rejection of Claims 1-3, 5-7, 9, 11, and 14 under 35 U.S.C. §112, First Paragraph, is Partly Rendered Moot, Partly Traversed, and Partly Accommodated

The Examiner has rejected claims 1-3, 5-7, 9, 11 and 14 under 35 U.S.C. §112, first paragraph (pp. 7-8). Applicants respectfully disagree. The Examiner alleges:

> The specification discloses a protein of SEQ ID NO: 1 and a nucleic acid sequence of SEQ ID NO: 2 that encodes the protein of SEQ ID NO: 1. However, claims 1 and 2 recites the protein of SEQ ID NO: 1 and its homologues and fragments, whereas claims 3 and 14 recite a DNA that encodes the protein of claim 1 or hybridises to the DNA encoding the protein of claim 1. Claims 5-7, 9, and 11 depend, either directly or indirectly, from claim 1. The claims do not require that the proteins and nucleic acids possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of protein and its homologues or a genus of DNA molecules.
>
> To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in claim 1 and 2 is a partial structure in the form of a recitation of "substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1". The specification asserts that the substantially the same amino acid sequence includes an amino acid sequence having at least about 50% homology, preferably at least 70% homology, more preferably at least 80% homology...."

> (pages 13 and 16 of the specification). Likewise, the only factor present in claim 14 is a mere chemical property of the DNA in the form of a recitation of 'hybridize to DNA encoding the protein of SEQ ID NO: 1 or its homologues. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.
>
> Therefore, only the protein of SEQ ID NO: 1 and the DNA encoding the protein (including SEQ ID NO: 2), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. (Pp. 7-8, par. 12.)

Applicants wish to draw the Examiner's attention to the state of the art at the time the application was filed, as evidenced by the Wong reference. Applicants have already discussed Wong at length, *supra*, and this discussion also applies to this rejection.

Moreover, claim 1 has been amended to read as follows:

> 1 (currently amended). An isolated protein which comprises the amino acid sequence represented by SEQ ID NO: 1, or a salt thereof.

Applicants respectfully submit that the amendment to claim 1 overcomes the present rejection and places claim 1 in condition for allowance. The isolated protein of claim 1 now comprises the amino acid sequence represented by SEQ ID NO: 1 or a salt thereof. Claims 3, 5-7, 9, 11, and 14 are dependent on claim 1 or on claims dependent on claim 1, and the same arguments apply to them accordingly.

In order to further prosecution in a timely manner, claim 2 has been cancelled without prejudice to their pursuit in an appropriate continuation or divisional application.

Applicants respectfully submit that claims 1, 3, 5-7, 9, 11, and 14 fulfill the requirements under 35 U.S.C. §112, first paragraph, and that these claims are in condition

for allowance. Applicants respectfully request the Examiner's reconsideration of these claims accordingly.

VIII. The Rejection of Claims 1-3, 5-7, 9, 1l, and 14 Under 35 U.S.C. §112, Second Paragraph, is Accommodated and Partly Rendered Moot

The Examiner has rejected claims 1-3, 5-7, 9, 11, and 14 under 35 U.S.C. §112, second paragraph (p. 9; par. 13). The Examiner alleges:

> Claim 1 is indefinite because it recites the term "substantially the same". Since neither the art nor the specification provides an unambiguous definition for the term, the claim is indefinite.
>
> Claim 9 provides for the use of the protein of claim 1, but since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.
>
> Claim 9 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki,* 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner,* 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).
>
> Claim 14 is indefinite because it recites "under highly stringent conditions", but without giving the conditions in the claim. Since neither the art nor the specification provides an unambiguous definition for the term, the claim is indefinite.
>
> Claims 2, 3, 5-7, and 11 depend, either directly or indirectly, from claim 1. (P. 9; par. 13.)

The present language of claims 1, 9, and 14 reads as follows:

1 (currently amended). An isolated protein which comprises the amino acid sequence represented by SEQ ID NO: 1, or a salt thereof.

9 (currently amended). A method of determining a ligand to the protein or its salt according to claim 1, which comprises

a. providing the protein according to claim 1or its salt;
b. providing a test substance;
c. exposing the protein or its salt to the test substance;
d. measuring either
   i. the binding of the test substance to the protein or its salt; or
   ii. the reactivity of the test substance to the protein or its salt.

14 (currently amended). An isolated DNA which hybridizes to the DNA according to claim 3 and hybridizes to the DNA according to claim 3 in a solution having a sodium concentration of no higher than 19mM at a temperature of at least 65°C.

Applicants respectfully submit that the present language of claims 1, 9, and 14 fully complies with the definiteness requirement. In order to further prosecution in a timely manner, claim 2 has been cancelled without prejudice to its pursuit in an appropriate continuation or divisional application. Claims 3, 5-7, and 11 depend, either directly or indirectly, on claim 1.

Applicants also respectfully submit that the present amendments to claims 1, 9, and 14 accommodate the Examiner's rejection of these claims under 35 U.S.C. §112, first paragraph, thereby placing claims 1, 3, 5-7, 9, 11, and 14 in condition for allowance.

IX. The Rejection of Claims 1-7, 9, 11, and 14 Under 35 U.S.C. §102(e) Is Traversed and Partly Rendered Moot

The Examiner has rejected claims 1-7, 9, 11, and 14 under 35 U.S.C. §102(e) "as being anticipated by Chen et al. (US 2003/0148450 A1, published on August 8, 2003; priority date, February 26, 1999)." Applicants respectfully disagree.

The Examiner alleges:

> Chen et al. teach a human orphan G protein coupled receptor with an amino acid sequence being 99.9% identical to SEQ ID NO: 1 and the cDNA that encodes the receptor protein (see attached sequence alignment). This cDNA, which has 53.6% match with SEQ ID NO: 2 (from nucleotide No. 354 to nucleotide No. 1649) with 99.9% similarity, would hybridize to SEQ ID NO: 2. Chen et al. also teach a vector and a host cell comprising the cDNA that encodes the receptor protein, as well as a method of producing the receptor protein (see, e.g., claims 73-76; Example 2). Thus, the reference of Chen et al. meets the limitations of claims 1-7, 9, 11, and 14. (P. 10; par. 15.)

Applicants respectfully disagree with the Examiner's comments and traverse the anticipation rejection.

As noted, supra, the present language of claim 1 reads as follows:

> 1 (currently amended). An isolated protein which comprises the amino acid sequence represented by SEQ ID NO: 1, or a salt thereof.

Applicants respectfully submit that a rejection under §102(e) requires the reference to contain each and every element of the rejected claim.

The cited Chen reference does not contain a description or suggestion of the amino acid sequence represented by SEQ ID NO: 1, according to the present language of claim 1. Nor is the claimed invention of claim 1 rendered obvious by this reference.

Claims 3-7, 9, 11, and 14 are dependent on claim 1 or on claims dependent on claim 1, and the same arguments likewise apply to these claims.

In order to further prosecution of the application in a timely manner, claim 2 has been cancelled without prejudice to its pursuit in an appropriate continuation or divisional application.

Accordingly, the Chen reference does not anticipate claims 1, 3-7, 9, 11, or 14 of the present application.

Applicants respectfully submit that the present claims 1, 3-7, 9, 11, and 14 fulfill the requirements of 35 U.S.C. §102(e) and request the Examiner's reconsideration of these claims accordingly.

X. The Objections to Claims 7, 9, and 11 Are Accommodated

The Examiner has objected to claims 7, 9, and 11 as follows:

> Claims 7, 9, and 11 are objected to under 37 CFR 1.75(c) as being in improper multiple dependent form because a multiple dependent claim should refer back to a preceding claim in the alternative only. See MPEP § 608.01(n).

Applicants have amended claims 7, 9, and 11 in accordance with the Examiner's objections and respectfully submit that claims 7, 9, and 11 are in condition for allowance. Applicants request the Examiner's reconsideration of these claims accordingly.

XI. The Prior Art Made of Record is Acknowledged

Applicants thank the Examiner for bringing Chen et al. (US 2003/0175891) to their attention.

XII. Conclusion

It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants hereby request a three-month extension of time for the Amendment and accompanying materials. If an additional extension of time is required, Applicants hereby request the Examiner to consider this a conditional petition for an extension of time. Although it is not believed that any additional fee (in addition to the fee concurrently submitted) is required to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

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